REMARKS

Claims 1, 3-12, 15, 16, 18-26 and 69 remain before the Examiner for reconsideration. Claims 3-14, 17, 27-68, and 70-103 have been withdrawn. Claim 2 has been canceled without prejudice.

In the Office Action dated November 30, 2007 the Examiner indicated that the amendments claims to the claims were entered. Specifically, the Examiner indicated that:

> Any rejection from the previous office action filed 01/26/2007 not addressed below has been withdrawn.
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> Applicant's election with traverse of Group I claims 1-12,15-16,18-26 and 69 in the reply filed on 10/11/2007 is acknowledged. The traversal is on the ground(s) that functionalizing a diamine into the corresponding isocyanate is not a recited method step in the claims. Also applicants assert that a search for groups I and II will require a search of the same art and points to the fact that the examiner searched for groups I and II in the previous action. Thus applicants surmise it would not be burdensome for the examiner to search the groups identified above. These arguments are not found persuasive because firstly applicants have amended their claims from the previous office action so that the multifunction isocyanate group is formed via amide conversion. This new limitation must be addressed in the method to produce the polyurethane (group II) but since it is a product by process type of limitation for the product claims (group 1), the patentability is determined on the product itself not on the process of its manufacture. The examiner disagrees with applicant's statement that functionalizing a diamine into the corresponding isocyanate is not a recited method step in the claims; clearly this is a step in making the isocyanate which is then reacted with the bioactive agent. Since the claims are drawn to a method of producing a polyurethane any step included in the claim language that is an active step in the process of manufacture must be treated as a limitation by the examiner.
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> The requirement is still deemed proper and is therefore made FINAL.

Applicants hereby confirm the election of the claims of Group I.

Claims 1,3-4,7-8,10,15-16,19 and 69 are rejected by the Examiner under 35 U.S.C. 102(b) "as being anticipated by Chen et al. (Xiangjiao Gongye 1997, 20(4), 244, cited by applicants)." Specifically, the Examiner asserted that:

> Chen teaches biodegradable polyurethanes modified by starch, the polyurethane was synthesized from the polyol poly(tetramethylene oxide), TDI (toluene diisocyanate) and starch which reads on the bioactive agent (polysaccharide) claimed by applicant. Regarding claims 3-4 starch and poly(tetramethylene oxide) each contain more than one

> hydroxyl group. Regarding the limitations within claim 1 on how the isocyanate is formed and within claims 7-8 which detail how the diisocyanate and bioactive come into contact with each other, these limitations are all product by process type of limitations, therefore since the product produced in Chen is the same as applicants claimed invention the limitations are considered met. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Regarding claim 10, since the scope of the active ingredient of Chen overlaps the actives of applicants claimed invention (polysaccharides) it is the position of the examiner that the same compound will have the same effects on the human body. Regarding the limitations within claims 15-16, starch besides reading on applicant's active agent is also a polyol that is a biomolecule, therefore it meets applicants limitations for claims 15-16.

Applicants respectfully traverse the Examiner's rejection.

Chen does not disclose or suggest a polyurethane formed by reacting isocyanate groups of at least one multifunctional isocyanate compound, wherein the multifunction isocyanate compound is derived from an aliphatic compound having at least two amine groups or a biomolecule having at least two amine groups with at least one bioactive agent having at least one reactive group –X which is a hydroxyl group (-OH) or an amine group ($-NH_2$) in a solution with water. To the contrary, Chen discloses a polyurethane elastomer formed by reacting poly(tetramethylene oxide), starch and toluene diisocyanate (TDI), an aromatic isocyanate. Moreover, the polyurethane compositions of the present invention are biodegradable within a living organism to release the bioactive agent, wherein the released bioactive agent affects at least one of biological activity or chemical activity in the host organism. There is no disclosure or suggestion within Chen of degradation of the polyurethanes thereof to release starch or any other bioactive agent within a living organism. Chen does not anticipate the present invention.

The Examiner also rejected Claims 1,3,7-8,10-12,19-22,27,34-35 and 69 under 35 U.S.C. 102(b) "as being anticipated by Lipatova et al. (Macromol. Symp. 152,139-150 (2000), cited previously)" . Specifically, the Examiner asserted that:

> Lipatova teaches hemocompatable (same as biocompatible) and biodegradable polyurethanes containing bioactive heparine fragments, which are prepared from diisocyanates, oligoetherglycols, chain extenders and heparin, which comprises a plurality of hydroxyl groups and has a therapeutic effect in the body. See pag 145-148 2r'd paragraph. The biocompatible and biodegradable polyurethanes containing bioactive

heparine fragments were used for the creation of artificial blood vessels. Regarding the limitations within claim I on how the isocyante is formed and within claims 7-8 which detail how the diisocyanate and bioactive come into contact with each other, these limitations are all product by process type of limitations, therefore since the product produced in Lipatova is the same as applicants claimed invention the limitations are considered met. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Regarding claim 3 heparin contains numerous hydroxyl groups. Regarding claim 11, Lipatova does anticipate a carbohydrate bioactive (heparin) but heparin also anticipates an anticancer agent as evidenced by the teaching of Niers et al. (Mechanisms of heparin induced anti-cancer activity in experimental cancer models, Grit. Rev. Oncol./Hematol. (2006), doi:10.1016/ j.critrevonc.2006.07.007), cited previously. Neirs clearly notes that heparin demonstrated anti-cancer activity in animal tumors, thus heparin meets the limitation that the bioactive agent is an anticancer agent. See entire document.

In response to Applicant's arguments filed 10/11/2007, the Examiner indicated that the arguments have been fully considered but they are not persuasive. Specifically, the Examiner asserted that:

Applicants assert that it is not apparent from Lipatova that the heparin itself is reacted with the multifunctional isocyanate. Applicants further assert that it would be impossible from the disclosure of Lipatova to ascertain if heparin would be a degradation product and how long such a degradation would take place and there is no disclosure within that heparin would be released into the body. Applicants further assert that heparin is incorporated in the polymer to improve hemocompatibility of the polymer itself and is not used for any biological effect after degradation. Applicants lastly assert that the new limitation which produces the multifunctional isocyanates from a biocompatible compound having two amine groups to isocyanate groups further differentiates their invention from Lipatova.

The relevance of these assertions is unclear. Applicant's claims are drawn to a polyurethane composition, therefore the patentability is determined on the product itself not on the process of its manufacture. Thus the starting material used to produce the diisocyantes and how the bioactive agent and isocyanates are reacted bear no weight on the patentability of the claimed subject matter if a product such as the polyurethanes of Liptova anticipates applicants claimed composition. Since Lipatova teaches polyurethane containing the bioactive heparin incorporated into its backbone, Lipatova anticipates applicants claimed invention. Regarding applicant's assertion that it would be impossible to determine if heparin would be a degradation product and if it would be released into the body, since Lipatova anticipates applicants claimed composition the examiner assumes that it must be capable of biodegrading and releasing the bioactive within a living organism. Besides the recitation that the polyurethane composition releases a bioactive agent within the body by degradation is an intended use type of limitation for the composition. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in

> order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Applicants respectfully traverse the Examiner's rejection.

Lipatova does not disclose or suggest a polyurethane formed by reacting isocyanate groups of at least one multifunctional isocyanate compound, wherein the multifunction isocyanate compound is derived from an aliphatic compound having at least two amine groups or a biomolecule having at least two amine groups, with at least one bioactive agent having at least one reactive group --X which is a hydroxyl group (-OH) or an amine group (-NH_2) in a solution with water. To the contrary, Lipatova discloses specifically only toluene diisocyanate (TDI), an aromatic isocyanate. Polyurethanes formed from such aromatic isocyanates do not degrade by the same mechanism as polyurethanes formed from the isocyanate compounds derived from aliphatic compounds as set forth in the present invention. The polyurethane compositions of the present invention are biodegradable within a living organism to release the bioactive agent, wherein the released bioactive agent affecting at least one of biological activity or chemical activity in the host organism. There is no disclosure within Lipatova of release of heparin or any other bioactive agent within a living organism. Indeed, given the known mechanisms of degradation of polyurethanes formed from aromatic isocyanate and oligoetherglycols (as set forth in Lipatova), heparin is not likely to be released upon degradation of the polyurethanes of Lipatova. Lipatova does not anticipate the present invention.

Claims 1,3-12,15-16,19-20,22,25 and 69 are rejected by the Examiner under 35 U.S.C. 102(e) "as being anticipated by Beckman et al. (US 7,264,823 B2)." Specifically, the Examiner asserted that:

> The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under. 37 CFR 1.131.
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> Beckman teaches an adhesive containing the reaction product of a multifunctional isocyanate reactant and at least one multifunctional reactant that can be selected from PEG, steroids, polysaccharides, saccharides, polyamino-acids such as proteins and/or peptides; the polymeric network formed is biocompatible and biodegradable. See abstract, col. 3 lin 14-col 4 lin 55 and claim 1. Regarding the

> limitation within claim 1 that the isocyanate is formed via conversion of two amine groups, the diisocyanate of Beckman was synthesized from lysine which contains two amine groups. Regarding claim 3 saccharides and polysaccharides contain numerous hydroxyl groups, thus meeting the claim limitation. Regarding claim 4 PEG is a polyol that contains two hydroxyl end groups, thus meeting the claim limitation. Regarding claims 5-6 Beckman teaches the use of a chain extender selected from tyrosine, lysine or tryptophan, all of which have at least two functional groups selected from hydroxyl or amine groups. See col 8 lin 56-col 9 lin 3. Regarding the limitations within claims 7-8 which detail how the diisocyanate and bioactive come into contact with each other, this limitation is a product by process type of limitations, therefore since the product produced in Beckman is the same as applicants claimed invention the limitations are considered met. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the some as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Regarding claim 10, since the scope of the active ingredients of Beckman overlaps the actives of applicants claimed invention (polysaccharides, peptides, proteins, steroids) it is the position of the examiner that the same compound will have the same effects on the human body. Regarding the limitations within claims 15-16, polysaccharides and saccharides besides reading on applicant's active agent are also polyols that are biomolecules, therefore applicants limitations for claims 15-16 are met. Regarding claim 20 it is inherent that since the peptides of Beckman are typically between 2-50 amino acids in length the peptide weight would fit within applicants broadly claimed MW. Regarding claim 22 Beckman's polymers did form foams, thus meeting the limitation of the claim. See col 8 lin 21-57. Regarding claim 25 Beckman teaches that the product has an average isocyanate functionality of at least 2.1, thus the ratio of NCO:OH must be greater than unity because there are still unreacted isocyanate groups left after the reaction of the diisocyanate with the multi-functional reactant.

Applicants respectfully traverse the Examiner's rejection.

Beckman et al. discloses an adhesive which includes isocyanate functionality that reacts with tissue and/or moisture surrounding tissue to adhere tissue. The adhesives of Beckman et al. are formed in the absence of water. See, for example, Examples 1 through 10. In that regard, the presence of water would cause reaction of the isocyanate functionality of the compounds of Beckman et al. and thereby render the compounds of Beckman et al. ineffective as adhesives. To the contrary, in the present invention, multifunction isocyanate compound are reacted with at least one bioactive agent in a solution with water. There is no disclosure or suggestion in Beckman et al. of reacting multifunction isocyanate compounds with at least one bioactive agent in a solution with water. Beckman et al. does not anticipate the present invention.

The Examiner also rejected Claims 1,3-4,7-8,12,19,22,27-30,33 and 69 under 35 U.S.C. 102(e) "as being anticipated by Woodhouse et al. (US 6,221,997 B1, cited previously)." Specifically, the Examiner asserted that:

> Woodhouse teaches biodegradable polyurethane materials synthesized from an amino acid based diisocyanate such as lysine, a polyol and an amino-acid chain extender (including more than one amino acid joined in a chain to form an oligopeptide). See col 2 lin 21-col 3 lin 30, col 6 lin 17-col 7 lin 5 and col 8 lin 20-39. The amino acids have a plurality of reactive amine groups. Regarding the limitations within claim 1 on how the isocyante is formed and within claims 7-8 which detail how the diisocyanate and bioactive come into contact with each other, these limitations are all product by process type of limitations, therefore since the product produced in Woodhouse is the same as applicants claimed invention the limitations are considered met. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

In response to Applicant's arguments filed 10/11/2007, the Examiner indicated that the arguments have been fully considered but they are not persuasive. Specifically, the Examiner asserted that:

> Applicants assert that Woodhouse does not disclose or suggest reacting isocyanate groups of a least one diisocyanate with at least one bioactive compound. Applicants support this assertion by pointing to the embodiments within Woodhouse in which ester linkages are introduced adjacent to the amino-acids. Applicants also assert that the amino acids may be altered or destroyed during enzymatic recognition and thus not be released into the body upon degradation of the polymer. Applicants lastly assert that Woodhouse only specifically describes reaction/esterfication of L-phenylalanine and L-lysine and 1,4-cyclohexane dimethanol to form a chain extender for use in the polyurethanes. Therefore applicants surmise that Woodhouse is not enabling for the use of such oligopeptides or polyaminoacids in the polyurethanes thereof.
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> The relevance of these assertions is unclear. Woodhouse clearly recites that the polyurethane is formed by reaction of the diisocyanate with the chain extender which is an amino acid that contains free amino end units. It is inherent that since a reaction would form polyurethane the diisocyanate reacted with the end groups on the amino acid chain. The ester linkages which are introduced adjacent to the amino acid chain applicants are referring to is just one of several embodiments and does not limit the scope in its entirety for the disclosure of Woodhouse. Regarding applicant's assertion that the amino acids may be altered or destroyed when they are recognized by the enzyme, since Woodhouse anticipates applicants claimed composition the examiner assumes that it must be capable of biodegrading and releasing the bioactive within a living organism. Besides the recitation that the polyurethane composition releases a bioactive agent within the body by degradation is an intended use type of limitation for

> the composition. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Regarding applicants assertion that Woodhouse only exemplifies esterfied chain extenders that include the amino acids, the examples within Woodhouse were given solely for the purpose of illustration and were not to be construed as being limiting to their invention since many variations are possible without departing from the spirit and scope of the invention.

Applicants respectfully traverse the Examiner's rejection.

In the present invention, multifunction isocyanate compounds are reacted with at least one bioactive agent in a solution with water. There is no disclosure or suggestion in Woodhouse et al. of reacting multifunction isocyanate compounds with at least one bioactive agent in a solution with water. Indeed, in the case of the polyurethanes of Woodhouse et al., water is considered a contaminant that would negatively impact the mechanical properties of the polyurethanes of Woodhouse et a. See, for example, Col. 14, line 62 to Col. 15, line 11. Woodhouse et al. does not anticipate the present invention.

Claims 1,3-12,15-16,18-26 and 69 are also rejected by the Examiner under 35 U.S.C. 103(a) "as being unpatentable over Zhang et al. (Biomaterials 21 (2000) 1247-1258, cited previously) in view of Liptova et al. (Macromol. Symp. 152, 139-150 (2000), cited previously) or in view of Woodhouse et al. (US 6,221,997 BI, cited previously)". Specifically, the Examiner asserted that:

> Zhang discloses biodegradable peptide-based urethane polymers synthesized by lysine diisocyanate (LDI) ethyl ester and glycerol (hydroxylated biomolecule) which were further reacted with water as the chain extender, forming foams for tissue engineering applications, the foams supported the growth of rabbit bone marrow stomal cells in vitro. See entire article. Regarding claim 23 the limitation of pore size is met by Zhang's discloser that the pore size can be 10 pm to 2 mm in diameter. See page 1252, right col. 2`d paragraph. Zhang disclosed that the free isocyanate content is 1.26% meeting the limitation on the free isocyanate content within claims 24 and 36. See page 1252 right col. 1st paragraph. Regarding claims 25-26 and 37-38 the NCO:OH equivalent limitations are met because Zhang discloses that 55 mmol of glycerol was added to 87 mmol of LDI, since LDI has two reactive sites (NCO) and ,lycerol has three (OH) the NCO:OH equivalent is 1.05.
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> Zhang while disclosing the peptide based urethane polymer may allow incorporation of proteins of interest such as cell attachment and/or growth factors does not give any working examples.

> Liptova and Woodhouse are disclosed above. Woodhouse and Liptova are used to primarily show that it was already well known in the art at the time of the invention to incorporate bioactive ingredients (heparin and polyamino acids) into biodegradable polyurethane/polyol polymers.
>
> Therefore it would have been obvious to one of ordinary skill in the art from the disclosure of Zhang to incorporate bioactive substances in the disclosed urethane polymers and from the disclosures of Liptova and Woodhouse it would have been obvious that polyurethanes could be conjugated to bioactive substances such as peptides and heparin. Thus the claimed invention would have been prima facie obvious since all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

In response to Applicant's arguments filed 10/11/2007, the Examiner indicated that the arguments have been fully considered but they are not persuasive. Specifically, the Examiner asserted that:

> Applicant's arguments filed 10/11/2007 have been fully considered but they are not persuasive.
>
> Applicants assert that for the reasons addressed above in applicant's arguments over the 102 (b) rejection over Liptova that the reference cannot cure the deficiencies of Zhang.
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> Since the arguments are essentially the same as above the examiner incorporates his remarks from above herein. As cited above Litova does read on applicants claimed polyurethanes containing a bioactive agent.

Applicants respectfully traverse the Examiner's rejection.

The Examiner admits that Zhang et al. is not enabling for covalent attachment of proteins within the polyurethane thereof. Once again, Zhang does not disclose even what is meant by incorporation of proteins. In that regard, in the present invention an isocyanate group of at least one multifunctional isocyanate compound is reacted with the bioactive agent in solution with water, thereby covalently bonding the bioactive agent within the polyurethane composition. There is no disclosure or suggestion in Zhang et al. of the reaction of a protein or any other bioactive agent in solution with water with a multiisocyanate compound to from a polyurethane which is biodegradable to release the bioactive agent within a living organism.

For the reasons set forth above, neither Lipatova not Woodhouse et al. overcome the deficiencies of Zhang et al.

The Examiner rejected Claims 1,3-4,7-12,15-16,19,25 and 69 on the ground of nonstatutory obviousness-type double patenting "as being unpatentable over claim 1 of U.S. Patent No. 7,264,823 B2." Specifically, the Examiner asserted that:

> Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1,3-4,7-12,15-16,19,25 and 69 are generic to all that is recited in claims 1 of U.S. Patent No. 7,264,823 B2. That is, claims 1 of U.S. Patent No. 7,264,823 B2 falls entirely within the scope of claims 1,3-4,7-12,15-16,19,25 and 69 or in other words, claims 1,3-4,7-12,1516,19,25 and 69 are anticipated by claims 1 of U.S. Patent No. 7,264,823 B2. Specifically both while not being identical in that applicant's claims are drawn to a polyurethane composition while `823 claims a method of applying a composition, both recite a polymer formed from reacting a multifunctional isocyanate reactant with a multifunctional reactant, the reactants claimed as detailed in the 102(e) rejection over Beckman above overlap in scope. Thus applicant's claimed invention is obvious and unpatentable over claim 1 of U.S. Patent No. 7,264,823 B2.

For the reasons set forth above, Applicants respectfully traverse the Examiner's rejection. Beckman et al. does not disclose or suggest the present invention.

In view of the above amendments and remarks, Applicants respectfully requests that the Examiner, indicate the allowability of the Claims, and arrange for an official Notice of Allowance to be issued in due course.

Respectfully submitted,
ERIC J. BECKMAN et al.

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By /Henry E. Bartony, Jr., Reg. No. 34,772/
Henry E. Bartony, Jr., Esq.
Reg. No. 34,772

Bartony & Hare, LLP
1806 Frick Building
437 Grant Street
Pittsburgh, Pennsylvania 15219-6101
412-338-8632 (telephone)
412-338-6611 (fax)
Attorney for Applicant